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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,824	09/08/2003	Stephen I. Rennard	UNMC/03017/0008	7805

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EXAMINER

AFREMOVA, VERA

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,824	RENNARD ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 February 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/21/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 11-19 as amended (2/21/2006) are pending and under examination.

Information Disclosure Statement

The missing copies of the references 3 and 4 (IDS filed 1/04/2004) were not provided. Therefore, the information disclosure statement filed 1/05/2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered in full.

Claim Rejections - 35 USC § 112

Claims 11-19 as amended remain/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 as amended is rendered indefinite by recitation of “substantially homogenous populations” of fibroblasts in the lack of definitions about how much and/or what % is intended for the claimed term “substantially homogenous populations”.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 11-14 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2003/0119107 (Dang et al).

Claims are directed to a method for producing fibroblasts wherein the method comprises step of obtaining embryonic stem (ES) cells, step of culturing ES to form embryoid bodies (EB), step of isolating EB, step of casting EB in a culture medium in 3D scaffolding material that is a gel, step of growing EB in the 3D material thereby inducing differentiation to produce fibroblasts.

Some claims are further drawn to the use of differentiation-inducing “cytokines” including TGF beta or FGF.

US 2003/0119107 (Dang et al) discloses a method for generation of cells or for producing cells from spheroids or from embryoid bodies wherein the method comprises step of obtaining embryonic stem (ES) cells, step of culturing ES to form embryoid bodies (EB), step of isolating EB, step of casting EB in a culture medium in 3D scaffolding material that is 3% agarose gel and step of growing EB encapsulated into the 3D material in a stirred bioreactor, for example: see abstract, par. 0120, par. 0116. Thus, the cited patent teaches method that comprises identical active steps and identical structural element as required by the claimed method. Therefore, the cited method results in the production of identical cells within the intended meaning of the claimed phrase “thereby inducing differentiation of the embryoid bodies to produce substantially homogenous populations of fibroblasts”.

As applied to the claims 12-14 and 19 the cited document also teaches the use of differentiation-inducing cytokines (par. 0082) including the use of TGF beta or FGF for

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producing mesodermal cells (table 11) that include and/or would be fibroblasts accordingly applicants' description (see instant specification page 11. par. 0034, line 7).

Thus, the cited document anticipates the presently claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0119107 (Dang et al) taken with Dani et al. ["Differentiation of embryonic stem cells into adipocytes in vitro". Journal of Cell Science (1997), 110: 1279-1285] and US 6,576,464 (Gold et al.).

Claims 11-14 and 19 as explained above. Some claims are further drawn to extraction of differentiated cells from the 3D material by digestion and centrifugation and to culturing the digested cells in monolayer culture. Some claims are further drawn to the use of media with 2% serum at step of inducing differentiation of embryonic cells and with 10% for monolayer culture.

US 2003/0119107 (Dang et al) is relied as explained above for the disclosure of a method for controlled generation of cells from embryonic stem cell-derived embryoid bodies that are encapsulated into 3D scaffold material. US 2003/0119107 teaches that cells are released from the 3D material by digestion (par. 0160). The cited document US 2003/0119107 also teaches the use of differentiation-inducing cytokines (par. 0082) including the use of TGF beta or FGF for

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producing mesodermal cells (table 11) that include and/or would be fibroblasts accordingly applicants' description (see instant specification page 11. par. 0034, line 7).

The cited document US 2003/0119107 discloses that in most cases differentiation inducing additives and/or factors are added to the serum-containing medium (table 10) and the disclosed protocols of culturing ES and EB encompass the use of 15% and/or 20% serum (par. 010, 0114). US 2003/0119107 is lacking particular disclosure about 2% and 10% serum containing media.

However, the cited reference by Dani et al. discloses the use of 10% serum in differentiation media in the method for culturing and differentiating embryonic cells, formation of embryoid bodies (page 1280, col. 1, par. 3) and production fibroblast-like cells (page 1280 col. 2, par. 1, lines 17-18).

Further, US 6,576,464 teaches that differentiation of embryonic cells can be induced by withdrawal of serum or by substituting medium devoid of serum at the time of replating (col.16, lines 53-56). Thus, reduction of serum content in the medium intended for induction of differentiation would be an obvious protocol to ordinary skill practitioner at the time the claimed invention was made. One of skill in the art would have been motivated to reduce amount of serum for the expected benefits in inducing differentiation of embryonic cells as suggested by US 6,576,464. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments with respect to claim 2/21/2006 have been considered but are moot in view of the new ground(s) of rejection.

With regard to the issues under 112-1 raised in the last office action applicants argue that embryoid bodies stably differentiate into fibroblasts in the presence or in the absence of cytokines when embryoid bodies are cultured in the gel (response page 6, par/ 3, line 5-8). Thus, claim limitations drawn to the use of specific cytokines are not critical as argued and they do not bear any specific meaningful weight. The cited US 2003/0119107 clearly teaches culturing embryoid bodies embedded in the gel within the meaning of the instant claims and as argued.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

April 20, 2006

A handwritten signature in black ink, appearing to read 'V. Afremova', with a long horizontal flourish extending to the right.

VERA AFREMOVA

PRIMARY EXAMINER